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Xanthinuria: A Rare Case Report

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ABSTRACT

INTRODUCTION: Classical xanthinuria is an autosomal recessive hereditary disease which manifests as a result of deficiency of xanthine dehydrogenase which converts hypoxanthine, and xanthine into uric acid. Molybdenum cofactor deficiency, an inherited form of xanthinuria, causes hyperreflexia, microcephaly, and other central nervous system symptoms in newborns. Molybdenum cofactor deficiency, an inherited form of xanthinuria, causes hyperreflexia, microcephaly, and other central nervous system symptoms in newborns. The function of three different enzymes (xanthine dehydrogenase, aldehyde oxidase, and sulfite oxidase) depends on a molybdenum-containing cofactor that is congenitally defective in this disorder.

CASE REPORT: A full term female baby born to a $G_3P_1L_1A_1$ mother via normal vaginal delivery was referred from outside hospital on day of life 10 in view of one episode of convulsion on day 3 of life. Baby was screened for inborn errors of metabolism which revealed increased excretion of Xanthine in urine. MRI of brain was done which showed extensive areas of diffusion restriction involving bilateral cerebral hemispheres, bilateral corticospinal tracts and corpus callosum suggestive of Acute hypoxic ischaemic encephalopathy.

DISCUSSION: Because of enzymatic deficiency, xanthine dehydrogenase cannot be converted into uric acid which leads to increase in blood levels, and urinary excretion of hypoxanthine, and xanthine. Since these substances have a lower solubility in urine, they accumulate in the urinary system leading to formation of stones. Reduced or undetectable serum uric acid levels associated with MoCD are a result of the deficiency of xanthine dehydrogenase. Most of the patients with classical xanthinuria are asymptomatic, and in 30% of the cases urolithiasis develops.

CONCLUSION: Refractory seizures, encephalopathy, and the absence of radiologic signs of HIE a positive family history of perinatal asphyxia, and refractory seizures are contributors in newborn fatalities that demonstrate a significant tendency to develop xanthinuria. A thorough research regarding its prevalence and prognosis should be done.

Keywords: xanthinuria, autosomal recessive hereditary disease, newborn

INTRODUCTION

Classical xanthinuria is an autosomal recessive hereditary disease which manifests as a result of deficiency of xanthine dehydrogenase which converts hypoxanthine, and xanthine into uric acid. Molybdenum cofactor deficiency, an inherited form of xanthinuria, causes hyperreflexia, microcephaly, and other central nervous system symptoms in newborns. Severe metabolic acidosis and cerebral bleeding are two other symptoms

that have been documented. The function of three different enzymes (xanthine dehydrogenase, aldehyde oxidase, and sulfite oxidase) depends on a molybdenum-containing cofactor that is congenitally defective in this disorder. The MOCS1 or MOCS2 molybdenum cofactor gene mutation is to blame for this deficiency. Because (1) neurologic symptoms overwhelm the clinical presentation and (2) a lack of sulfite oxidase, which is required for the final stage in cysteine metabolism, results in death within the first year of life, xanthinuria is simply a marker in this context.[1]

In order to treat molybdenum cofactor deficiency (MoCD), substitution therapy using cyclic pyranopterin monophosphate (cPMP), a cofactor's biosynthetic precursor, was used in the study. According to the study's findings, cPMP replacement is the first treatment for patients with MoCD type A that is successful and has a good safety profile.[2] Although the death rate is unknown and unanticipated, renal failure complications that go undiagnosed or untreated can cause death. Acute renal failure, renal colic, hematuria, and/or urinary tract infection are among the signs of urolithiasis that nearly 40% of individuals with classic xanthinuria present with. Iatrogenic xanthinuria can occur during allopurinol therapy, which is used to reduce urine uric acid excretion in conditions with endogenous overproduction of uric acid. Inhibition of xanthine dehydrogenase by allopurinol may lead to accumulation and urinary excretion of xanthine. Patients with Lesch-Nyhan syndrome or patients with partial HGPRT deficiency have developed xanthine nephropathy, acute kidney failure, and stones following treatment with allopurinol. Moreover, about two thirds of patients are asymptomatic and present with an incidental finding of extremely low levels of uric acid in the blood.[4]

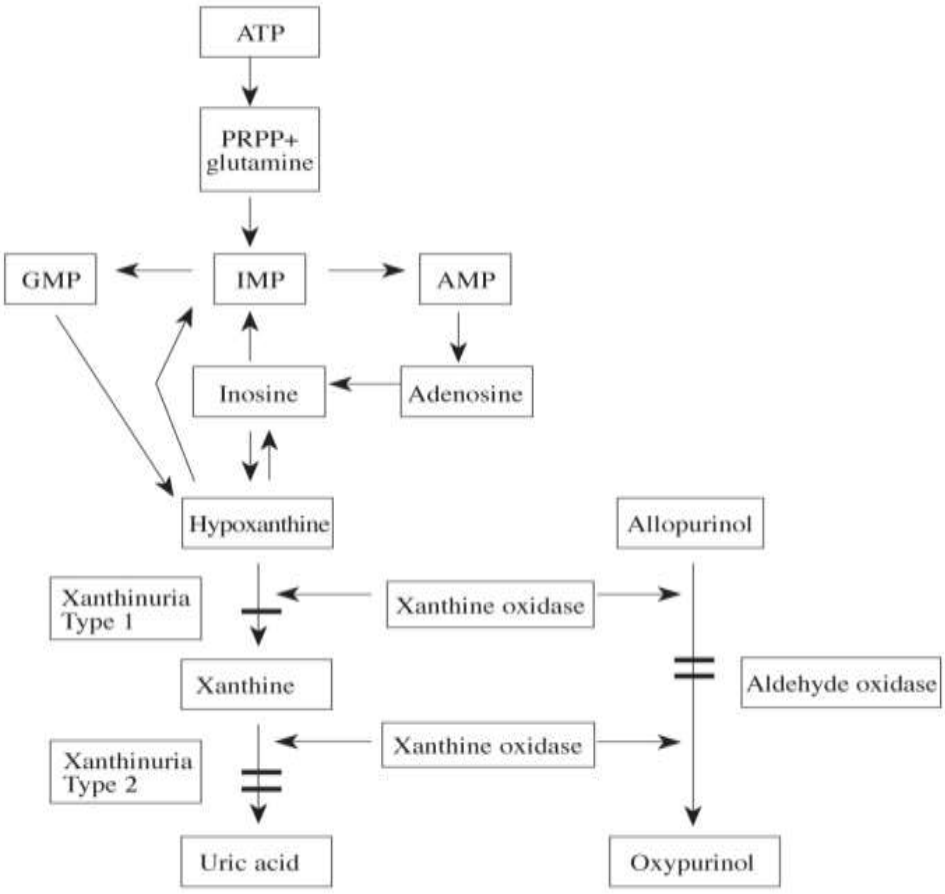

Figure 1: Discrimination between xanthinuria Types I (−), and II (=) in the xanthine –uric acid metabolic pathway AMP: adenosine monophosphate; IMP: inosine monophosphate; GMP: Guanosine monophosphate; PRPP: 5-phosphoribosylpirophosphate; ATP: adenosine triphosphate.

CASE REPORT

A full-term female baby born to a $G_3P_1L_1A_1$ mother via normal vaginal delivery was referred from outside hospital on day of life 10 in view of one episode of convulsion on day 3 of life. Baby had been started on two antiepileptics. Birth weight of baby was 2.7 kg which was appropriate for gestational age. Baby cried immediately after birth as informed by the relatives. Breastfeeding was started after 2 hours of life. On day 3 of life baby showed generalized tonic clonic convulsions with fisting and hypertonia. Seizures continued even after three antiepileptics, given at maximum tolerable doses. Baby was taken on O_2 by nasal prongs. Baby was kept NBM. IV inotropic (Inj.Dobutamine) and IV fluids were started. Convulsions stopped on day of life 7 after treatment with Midazolam infusion and Pyridoxine. CSF examination was within normal limits. There was elevated levels of lactate and ammonia. Baby was screened for inborn errors of metabolism which revealed increased excretion of Xanthine in urine. MRI of brain was done which showed extensive areas of diffusion restriction involving bilateral cerebral hemispheres, bilateral corticospinal tracts and corpus callosum suggestive of Acute hypoxic ischaemic encephalopathy. On day 8 of life, baby was given expressed breast milk through orogastric tube. Oromotor stimulation was started. Oral feeds were established followed by breastfeeding. Baby was shifted to motherside. Limb physiotherapy was given. USG abdomen & pelvis was done which was normal. ENT opinion was taken in view of stridor. Flexible endoscopy revealed Laryngomalacia grade 2. Eye examination was done which showed temporal avascular retina. Baby had no further episodes of convulsions. Antiepileptics were tapered. Single anticonvulsant with maintenance dose was continued. Multivitamins containing Pyridoxine and other supplements were given. Parents were counselled about the condition and no purine diet was advised. Baby was discharged and advised for follow up at neurophysician.

Fig 1: Neonate with c/o Xanthinuria

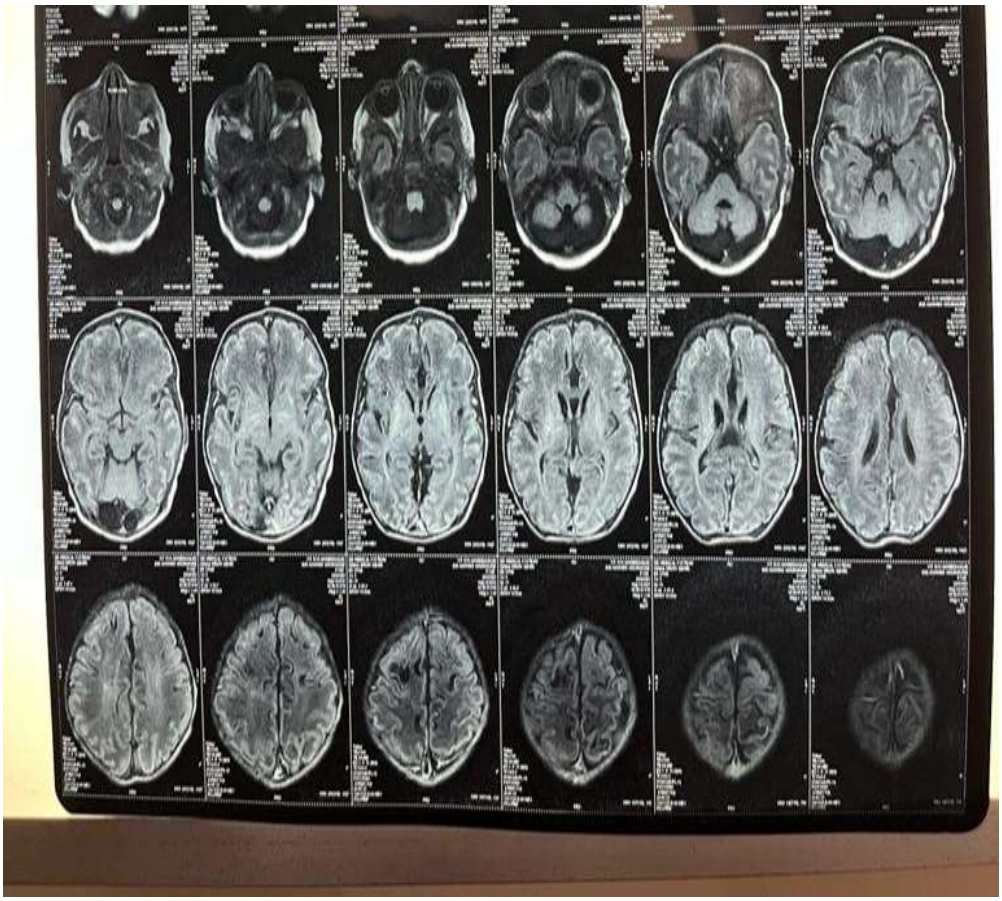

Fig 2: MRI of Brain showing hypoxic ischaemic encephalopathy changes

DISCUSSION

Classical xanthinuria develops as a result of deficiency of xanthine dehydrogenase (XDH) which converts hypoxanthine, and xanthine into uric acid as the last step of purine metabolism.[5] Because of enzymatic deficiency, xanthine dehydrogenase can not be converted into uric acid which leads to increase in blood levels, and urinary excretion of hypoxanthine, and xanthine. Since these substances have a lower solubility in urine, they accumulate in the urinary system leading to formation of stones.[6]

The catalytic activity of the enzymes xanthine dehydrogenase, sulfite oxidase, nitrogenases, and nitrate reductase depends on the presence of the molybdenum cofactor. Xanthine and hypoxanthine are transformed to uric acid. Abnormal sulfite buildup as a result of this. Excitotoxic neuronal death results from sulfite oxidase deficiency.[7] Reduced or undetectable serum uric acid levels associated with MoCD are a result of the deficiency of xanthine dehydrogenase.[8] Most of the patients with classical xanthinuria are asymptomatic, and in 30% of the cases urolithiasis develops.[9] In classical xanthinuria, blood, and urine uric acid levels are very low (<2 mg/100 mL), and they can be easily detected.[10] However, levels of hypoxanthine, and xanthine can be measured using high-performance liquid chromatographic (HPLC) methods employed for the detection of urinary, and blood amino acid levels.[11]

CONCLUSION

Refractory seizures, encephalopathy, and the absence of radiologic signs of HIE a positive family history of perinatal asphyxia, and refractory seizures are contributors in newborn fatalities that demonstrate a significant tendency to develop xanthinuria. As a result, the panel of tests used to evaluate newborns with refractory seizures and an encephalopathy

that isn't clear must include measuring the quantity of uric acid in the blood and urine. The treatment is nonspecific. Multivitamins containing pyridoxine may help. The prevalence of xanthinuria is unknown. A thorough research regarding its prevalence and prognosis should be done.

Declaration by Authors

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